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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SINGH, ANOOP KUMAR	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/767,064	PELED ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *201-243* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *201-243* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on January 29, 2004 has been received and entered. Claims 1-200 have been canceled. Applicants have added new claims 201-243.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 201, 209-215, 217-231, 235, 238 and 239, drawn to a method of expanding an ex-vivo population of hematopoietic stem cells and culturing said cells under conditions selected from the group consisting of conditions reducing expression and/or activity of CD38 by agent is a polynucleotide encoding an anti CD38, an anti retinoic acid receptor, an anti retinoid X receptor or an anti Vitamin D receptor intracellular antibody or in presence of nicotinamide or in presence of copper chelator, classified in class 435, subclass 375.

II. Claims 201, 215, 226 and 238-239, drawn to a method of expanding an ex-vivo population of hematopoietic stem cells and culturing said cells under conditions selected from the group consisting of conditions reducing expression and/or activity of CD38 is down regulated by PI-3 kinase antibody, classified in class 435, subclass 375.

III. Claims 208, 216, 232-234, 236-237 and 242-243 drawn to a transplantable hematopoietic cell preparation comprising an expanded population of hematopoietic stem cells propagated ex-vivo from hematopoietic mononuclear cells in the presence of an effective amount of an agent, selected from the group consisting of reducing expression and/or activity of CD38 in said mononuclear cells; and reducing an expression and/or activity of PI 3-kinase in said mononuclear cells; or an agent that is a copper chelator or, or nicotinamide, in mononuclear cells; while at the same time, substantially inhibiting differentiation of said

hematopoietic stem cells, and a pharmaceutically acceptable carrier, classified in class 435, subclass 325.

IV. Claims 202-203 and 207, drawn to method of transplanting or implanting hematopoietic cells, the method comprising: (a) obtaining hematopoietic mononuclear cells; (b) culturing said mononuclear cells ex vivo for cell proliferation, (c) transplanting or implanting said hematopoietic stem cells to a recipient, classified in class 435, subclass 325.

V. Claims 204-206, drawn to a method of genetically modifying hematopoietic stem cells with an exogene comprising: (a) obtaining hematopoietic mononuclear cells; (b) culturing said mononuclear cells ex vivo for cell proliferation and (c) genetically modifying said hematopoietic stem cells with the exogene, classified in class 424, subclass 93.1.

VI. Claim 240, drawn to an assay for determining whether a chelator causes induction of differentiation of hematopoietic stem cells, the assay comprising: culturing hematopoietic mononuclear cells in the presence of the chelator and monitoring differentiation of said hematopoietic stem cells, classified in class 435, subclass 4.

VII. Claim 241, drawn to an assay for identifying an effective hematopoietic stem cell expansion agent, classified in class 435, subclass 4.

Applicant is required to elect one polynucleotide sequence in claims 220-222 since each sequence has a distinct structure, encodes different protein that would have different function. This is a restriction requirement not an election of species.

The inventions are distinct, each from the other because of the following reasons:

Inventions of groups I-II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant

case, inventions of groups I-II are patentably distinct, each from other because each method uses material compositions that have distinct structure, function and utility. For example, the method of group I requires reducing the activity of CD38 by agents such as nucleic acid encoding retinoic acid receptor, while invention of group II requires PI-3 kinase antibody. It is noted that each method step requires distinct and different agent that has distinct and different chemical, physical structure. In addition, method of administering polynucleotide to the cells will different as compared to antibody or any other chemical agent, thus each condition and composition will work through independent mechanism. Therefore, searching for a different composition in different and distinct method steps will not be coextensive and would require separate and non-coextensive searches in the patent and non-patent literature.

Inventions of groups IV-V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, inventions of groups IV-V are patentably distinct, each from other because each method uses material compositions that have distinct structure, function and utility. For example, the method of group IV requires culturing of cell followed by implanting to the subject, while invention of group V requires culturing and then genetically modifying the cells which is not required by method of group IV. Therefore, each method steps in groups IV-VI would require materially different composition and use different steps. Therefore, searching for a different of different and distinct method steps will not be coextensive and would require separate and non-coextensive searches in the patent and non-patent literature.

Inventions I-II and III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, composition of group III can use other methods for expanding hematopoietic cell, while method of group I-II can be used for expanding

cells from other source. Therefore, searching of these inventions would impose an undue burden.

Inventions III and IV-V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the composition of group III can be used in culture of other cells, while other progenitor cell could be genetically modified for transplantation. Thus, groups II and III are related as product and process of use.

Inventions of groups VI-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, inventions of groups VI-VII are patentably distinct, each from other because each method uses material compositions that have distinct structure, function and utility. For example, the group VI requires culturing of cell in presence of a chelator to monitor differentiation, while invention of group VII requires identifying an agent that could enhance proliferation of hematopoietic cell. It is noted that each assay in groups VI-VII require materially different composition and is directed to accomplish different purpose by using different method steps. Therefore, searching for a different of different and distinct method steps will not be coextensive and would require separate and non-coextensive searches in the patent and non-patent literature.

Inventions of groups I-II, III, IV-V and VI-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, they are drawn to methods that have distinct steps, separate composition for practice and produce different product or results. For example, steps of expanding cell in different composition as claimed in inventions I-II cannot be used in transplanting method of group IV or genetically modifying cell as recited in group V or screening methods of groups VI-VII. Therefore, the inventions of group I-II,

III, IV-V and VI-VII are patentably distinct each from the other and will require separate and non-coextensive searches in the patent and non-patent literature.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Election of Species

This application contains claims directed to the following patentably distinct species: In the instant case, Applicants are required to elect specific species of condition wherein only the culturing steps have positive species such as culturing cells under conditions selected from the group consisting of conditions reducing expression and/or activity of CD38 in said mononuclear cells, conditions reducing capacity of said hematopoietic mononuclear cells in responding to retinoic acid, retinoids and/or Vitamin

D in said mononuclear cells, conditions reducing capacity of said hematopoietic mononuclear cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said mononuclear cells; culturing said mononuclear cells in the presence of nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite in said mononuclear cells; conditions reducing an expression and/or activity of PI 3-kinase in said mononuclear cells; and culturing said mononuclear cells in the presence of at least one copper chelator or chelate.

The species are independent or distinct because only the culturing steps have positive species and each culturing condition would be distinct and different, therefore applicants are required to elect only one culturing condition.

Applicant is required under 35 U.S.C. 121 to elect a single culturing condition as recited for claim 201, 202, 204, 207, 208, 241 and 242 disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 201, 202, 204, 207, 208, 241 and 242 are generic.

This application contains claims directed to the following patentably distinct species: hematopoietic mononuclear cells are derived from a source selected from the group consisting of bone marrow, peripheral blood and neonatal umbilical cord blood.

The species are independent or distinct because obtaining cells from each will involve patentably distinct method step. Therefore, searching for obtaining cell from one source will not yield result for other species.

Applicant is required under 35 U.S.C. 121 to elect a single source as recited for claim 209 disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 209 is generic.

This application contains claims directed to the following patentably distinct species of the claimed invention: group consisting of stem cell factor, FLT3 ligand, interleukin-1, interleukin-2, interleukin-3, interleukin-6, interleukin-10, interleukin-12, tumor necrosis factor-a and thrombopoietin.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 212 is generic.

This application contains claims directed to the following patentably distinct species of the claimed invention: group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor, erythropoietin, FGF, EGF, NGF, VEGF, LIF, Hepatocyte growth factor and macrophage colony stimulating factor.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 214 is generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of

record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

A search and examination of more than one invention and species as defined above would unduly burden the office. Each of the invention and species requires a different search of the art and concerns separate consideration of patentability. For example, the subject matter of many of the species is not largely co extensive as the inventions are related to distinct methods. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143). Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272- 0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anoop Singh, Ph.D.
Examiner, AU 1632